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EDITORIAL COMMENT

The Heart of the Matter

Prime Time E/e′ Prime!*

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If it were done, when 'tis done, then 'twere well
It were done quickly. If th' assassination
Could trammel up the consequence, and catch
With his surcease success; that but this blow
Might be the be-all and the end-all here,
—Shakespeare (1)

From perhaps the earliest description of diastole—"the atria or filling chambers contract together while the pumping chambers or ventricles are relaxing and vice versa"—by Leonardo da Vinci (1452 to 1519) to the more modern techniques, indexes, and innovative imaging tools of diastolic function, our understanding of left ventricular (LV) diastolic properties has continued to advance. Although Carl J. Wiggers (2) first proposed the term inherent elasticity to describe the passive properties of the heart, it was Kitabatake et al. (3) in 1982 who brought the study of diastole and disease to the forefront in their seminal article describing the transmitral flow velocity curves obtained with Doppler echocardiography in different disease states.

The past decade can aptly be called the decade of "diastology." We have made rapid advances in our understanding of LV filling dynamics, cardiovascular elastance, vascular and ventricular stiffness, as well as left atrial (LA) mechanics. New developments in echocardiography enable a much more comprehensive assessment of LV systolic and diastolic function, including measurement of myocardial deformation or strain, ventricular twist and untwist, annular motion (longitudinal function), and LV suction (4). Despite the publication of recommendations (5), the classification of diastolic stages continues to show variation between observers because conflicting findings are common and many patients fall "between" stages (6).

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Diastolic dysfunction (DD) grade Ia has been in use at the Mayo Clinic for more than 2 decades (7) and has recently been described in detail by Pandit et al. (8). In this issue of *iJACC*, Kuwaki et al. (9) make a substantial attempt to break the gridlock of the last several years by showing that the addition of this additional grade (using E/e′ ratio >10 as the defining element to differentiate grade I DD from grade Ia DD) to the existing classification of DD (5) improves intraobserver and interobserver agreement as well as providing prognostic information. In their study, Kuwaki et al. (9) were able to successfully classify 227 of the 1,362 patients (16.7%) who could not originally be classified into any DD grade into grade Ia. However, even after the introduction of this new grade, the investigators were unable to classify approximately 7% of this cohort of 1,362 patients into any DD grade—a demonstration of the palpable tension of assessing DD by echocardiography when key indices sometimes yield discrepant information. Of interest, Kuwaki et al. (9) also performed 2-dimensional speckle tracking analysis of LA (complete in 88% of the cohort) and found impaired LA strain and strain rates in accordance with the traditional DD grading system. LA mechanical properties (peak positive strain rate during systole, or SRs; peak negative strain rate during early diastole, or SRe) of grade Ia DD were similarly impaired to grade II DD, whereas peak negative strain rate during late diastole, or SRa, "LA booster function," was higher in grade Ia than in grade II. Thus, the E/e′ ratio in conjunction with LA volume/mechanics, represents the most efficient means of initial diastolic assessment.

In addition to the echocardiographic parameters to characterize diastology, Kuwaki et al. (9) have also

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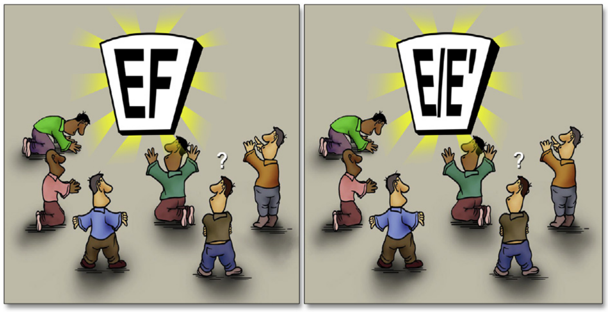

FIGURE 1 Barometers of Cardiac Function

This illustration depicts the 2 sentinel indices of the human heart—ejection fraction and E/e′ ratio (left atrial pressure)—that can be instrumental in stratifying patients into systolic and diastolic dysfunction with echocardiography. The illustration shows practitioners at 2 ends of the spectrum: those that reckon these indices as unalloyed parameters of cardiac function and those that question whether to believe them lock, stock, and barrel.

shown the interesting and noteworthy association between the new DD grade Ia and major adverse cardiac events. During the past decade, an increasing body of evidence has demonstrated that DD is associated with increased all-cause mortality, cardiovascular death, new-onset atrial fibrillation, sudden cardiac death, and hospitalization for heart failure (10). In addition, the clinical syndrome of heart failure associated with DD—heart failure with preserved ejection fraction—has been shown to carry a similar prognosis to heart failure with reduced ejection fraction (11). Kuwaki et al. (9) have shown that cardiac death and major adverse cardiac events rate for grades Ia and II are nearly identical and significantly worse than either grade I or those with normal diastolic function.

The study of Kuwaki et al. (9) is appealing due to the straightforward nature of the new grade of DD. Their study puts LV filling pressure (E/e′) at the epicenter of diastology, a parameter, which, in the average echocardiographic laboratory, is an easily acquired one. The E/e′ ratio (mitral inflow E-wave divided by annular tissue e′ wave) is among the most reproducible echocardiographic parameters to estimate mean pulmonary capillary wedge pressure, mean LA pressure, or mean LV diastolic pressure and is the preferred prognostic parameter in several cardiac conditions (5).

It has been demonstrated that E/e′ ratio is predictive of adverse events in hypertensive heart disease, in mitral regurgitation, in atrial fibrillation, after a myocardial infarction, in several cardiomyopathic processes, in end-stage renal disease, and even in the general community. This surrogate of mean LA pressure defines the hemodynamic health of the LV. The ability of this ratio to predict filling pressure has been demonstrated in patients with normal sinus rhythm, sinus tachycardia, preserved systolic function, atrial fibrillation, and in patients with hypertrophic cardiomyopathy (12).

This study does, however, have limitations. The Kuwaki et al. (9) have exclusively used the lateral e′ velocity to represent the mitral annular Doppler tissue velocity, excluding entirely the septal e′ velocity. This is a seminal preterition because the difference in the 2 can be exaggerated in several cardiac pathologies. Indeed, it is imperative to use the average of septal and lateral e′ velocities when drawing conclusions on LV filling pressures in patients with normal ejection fraction. Current guidelines (5) maintain that an average E/e′ ratio (septal and lateral) of <8 identifies patients with normal filling pressures, whereas a ratio >13 identifies those with increased filling pressures. When the ratio falls between these cutoffs, other echocardiographic measurements such as mitral inflow velocities, pulmonary venous flow velocities, pulmonary artery pressures, and LA volume index are necessary.

A major problem with DD is that it fails to attract the attention of the busy clinician in a "real world" practice setting because it lacks the mojo of ejection fraction—that virtual "be all and end all" of an echocardiographic report (**Fig. 1**). In addition, lack of correct understanding and consensus on the pathophysiology as well as the subsequent diagnostic/therapeutic strategies in DD contribute to this quandary. Besides, difficulty in studying and measuring the complex interplay of multiple inter-related events that contribute to diastolic filling of the LV remains a formidable task. However, continued development and assessment of noninvasive imaging modalities using tissue Doppler strain imaging, speckle tracking, 3-dimensional echocardiography, and high-resolution cardiac magnetic resonance imaging may finally contribute to a richer understanding of diastology. For now, we have to ask and answer the important question: is E/e′ ratio for diastole what ejection fraction is for systole, or is the E/e′ ratio the be-all and end-all of diastology?

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